CLAIMS

What is claimed:

1.   A polypeptide that binds APRIL comprising the sequence of Formula I:

$C-X_2-X_3-X_4-X_5-Y-X_7-D-X_9-L\ X_{11}-X_{12}-X_{13}-C-K-X_{16}-C-X_{18}-X_{19}-X_{20}-C\ -X_{22}-X_{23}-X_{24}-X_{25}\ -$
$X_{26}-X_{27}-X_{28}-X_{29}-C-X_{31}-X_{32}-X_{33}-C$ (Formula I)

wherein X_{11} is any amino acid residue except A;

wherein X_2, X_3, X_4, X_5, X_7, X_9, X_{11}, X_{12}, X_{13}, X_{16}, X_{18}, X_{19}, X_{20}, X_{22}, X_{23}, X_{24}, X_{25}, X_{26}, X_{27}, X_{28}, X_{29}, X_{31}, X_{32}, X_{33} are any amino acid except cysteine.

2.   The polypeptide according to claim 1, wherein X_{11} is L, I or V.

3.   The polypeptide according to claim 1, wherein X_{18} is selected from the group consisting of Q, D and A.

4.   The polypeptide according to claim 1, wherein if X_{20} is Y, then X_{18} is D.

5.   The polypeptide according to claim 1, wherein X20 is R.

6.   The polypeptide according to any one of claims 1-5, wherein the polypeptide comprises an amino acid sequence that is 85% or more identical to a CRD sequence of a native BCMA.

7.   The polypeptide according to claim 1, wherein the sequence of Formula I is selected from the group consisting of CSQNEYFDSLLHACKPCQLRCSSNTPPLTCQRYC, CSQNEYFDSLLHACKPCDLRCSSNTPPLTCQRYC, CSQNEYFDSLLHACKPCDLYCSSNTPPLTCQRYC, and CSQNEYFDSLVHACKPCQLRCSSNTPPLTCQRYC.

8.   A polypeptide that binds BAFF comprising the sequence of Formula II:

$C-X_2-X_3-X_4-X_5-X_6-X_7-D-X_9-L-X_{11}-X_{12}-X_{13}-C-X_{15}-X_{16}-C-X_{18}-X_{19}-X_{20}-C-X_{22}-X_{23}-X_{24}-X_{25}\ -$
$X_{26}-X_{27}-X_{28}-X_{29}-C-X_{31}-X_{32}-X_{33}-C$ (Formula II)

wherein X_6 is selected from the group consisting of Y, A, D, S and F;

wherein X_{11} is any amino acid residue except A;

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wherein X_{15} is any amino acid residue except A or K;

wherein X_{18} is selected from the group consisting of Q, D and A;

wherein X_{20} is selected from the group consisting of R, Y and A;

wherein X_2, X_3, X_4, X_5, X_7, X_9, X_{10}, X_{12}, X_{13}, X_{16}, X_{19}, X_{22}, X_{23}, X_{24}, X_{25}, X_{26}, X_{27}, X_{28}, X_{29}, X_{31}, X_{32} and X_{33} are any amino acid except cysteine; and

provided that the Formula II does not comprise the sequence CSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYC.

9.   The polypeptide according to claim 8, wherein X_{11} is L, I or V.

10.   The polypeptide according to claim 8, wherein X_{15} is I, V or A.

11.   The polypeptide according to claim 8, wherein X_{18} is D and X_{20} is Y.

12.   The polypeptide according to any one of claims 1-11, wherein the polypeptide comprises an amino acid sequence that is 85% or more identical to a CRD sequence of a native BCMA.

13.   The polypeptide according to claim 8, wherein the sequence of Formula II is selected from the group consisting of CSQNEAFDSLLHACIPCQLRCSSNTPPLTCQRYC, CSQNESFDSLLHACIPCQLRCSSNTPPLTCQRYC, CSQNEFFDSLLHACIPCQLRCSSNTPPLTCQRYC, CSQNEYFDSLLHACIPCDLRCSSNTPPLTCQRYC, CSQNEYFDSLLHACIPCQLYCSSNTPPLTCQRYC, and CSQNEYFDSLLHACIPCDLYCSSNTPPLTCQRYC.

14.   The polypeptide according to any one of claims 1 to 7, wherein the Formula I further comprises the sequence NSVKGT linked carboxy-terminal to the thirty-fourth residue.

15.   The polypeptide according to any one of claims 8 to 13, wherein the Formula II further comprises the sequence NSVKGT linked carboxy-terminal to the thirty-fourth residue.

16.   The polypeptides according to any one of claims 1-13, wherein the polypeptide comprises sequences N-terminal, C-terminal or both N-terminal and C-terminal to the sequence of Formula I or Formula II that are heterologous to a native BCMA polypeptide.

17.   A polypeptide that is a BCMA variant having an amino acid sequence derived from a mammalian BCMA polypeptide wherein at least one amino acid residue corresponding to the amino acid residue selected from the group Q10, E12, Y13, F14, I22, Q25 and R27 of FIG.5 is altered.

18.   The polypeptide according to claim 17, wherein the I22 has been substituted with K.

19.   The polypeptide according to claim 17, wherein the mammalian BCMA polypeptide is altered at a amino acid residue corresponding to I22 and an amino acid residue corresponding to any one of the residues F14 and Q25 of FIG.5.

20.   The polypeptide according to claim 17, wherein the mammalian BCMA polypeptide is altered at a residue corresponding to R27 and a residue corresponding to any one of the residues Y13 and Q25 of FIG.5.

21.   The polypeptide according to claim 17, wherein Q25 has been substituted with D and R27 has been substituted with Y.

22.   The polypeptide according to any one of claims 8-21, wherein the polypeptide comprises an amino acid sequence that is 85% or more identical to a CRD sequence of a native BCMA.

23.   The polypeptide according to any one of claims 1-22, wherein the polypeptide further comprises a leucine zipper.

24.   The polypeptide according to any one of claims 1-22, wherein the polypeptide is attached to a non-proteinaceous polymer.

25.   The polypeptide according to any one of claims 1-22, wherein the polypeptide is an immunoadhesin.

26.   The polypeptide according to any one of claims 1-22, wherein the polypeptide is an antibody.

27.   The polypeptide according to claim 26 wherein the antibody is selected from the group consisting of a F(ab) antibody, F(ab')$_2$ antibody and a scFv antibody.

28.   The polypeptide according to any one of claims 1-22, wherein the polypeptide is attached to an agent selected from the group consisting of a growth inhibitory agent, a cytotoxic agent, a detection agent, an agent that improves the bioavailability of the polypeptide and an agent that improves the half-life of the polypeptide.

29. The polypeptide according to claim 28, wherein said cytotoxic agent is selected from the group consisting of a toxin, an antibiotic and a radioactive isotope.

30. A nucleic acid molecule encoding the polypeptide according any one of claims 1-22.

31. A vector comprising the nucleic acid molecule according to claim 30.

32. A host cell comprising the nucleic acid molecule according to claim 30 or a vector comprising the nucleic acid molecule.

33. A composition comprising the polypeptide according to any one of claims 1-22, optionally further comprising a pharmaceutically acceptable carrier.

34. A composition comprising the polypeptide according to any one of claims 1-22, optionally further comprising a second therapeutic agent selected from the group consisting of an agent for treating an immune-related disease, a chemotherapeutic agent and a cytotoxic agent.

35. A method for producing a polypeptide comprising the step of culturing a host cell comprising the vector according to claim 31 under conditions suitable for expressing the polypeptide from the vector.

36. A method for identifying an inhibitor of APRIL binding to BCMA comprising the step of detecting an inhibitor that partially or fully blocks the binding of the polypeptide according to any one of claims 1-7 and 14 and APRIL.

37. A method for identifying an inhibitor of BAFF binding to BCMA comprising the step of detecting an inhibitor that partially or fully blocks the binding of the polypeptide according to any one of claims 8-13 and 15 and BAFF.

38. A method for inhibiting native APRIL binding to native BCMA comprising the step of contacting an APRIL polypeptide with the polypeptide according to any one of claims 1-7, 14 and 18.

39. A method for inhibiting native BAFF binding to native BCMA comprising the step of contacting a BAFF polypeptide with the polypeptide according to any one of claims 8-13, 15 and 21.

40. A method for inhibiting native APRIL and/or native BAFF binding to native BCMA comprising the step of contacting an APRIL polypeptide or a BAFF polypeptide with the polypeptide according to any one of claims 17-22.

41. A method for inhibiting native APRIL binding to native BCMA in a mammal comprising the step of administering the polypeptide according to any one of claims 1-7 and 14 in an amount effective to inhibit binding between APRIL and BCMA in the mammal.

42. A method for inhibiting native BAFF binding to native BCMA in a mammal comprising the step of administering the polypeptide according to any one of claims 8-13 and 15 in an amount effective to inhibit binding between BAFF and BCMA in the mammal.

43. A method for inhibiting native BAFF and/or native APRIL binding to native BCMA in a mammal comprising the step of administering the polypeptide according to claim 17-22 to the mammal.

44. A method for treating an immune-related disease in a mammal suffering from an immune disease comprising the step of treating the mammal with a therapeutically effective amount of the polypeptide according to any one of claims 1-22.

45. The method according to claim 44, wherein the immune related disease is selected from the group consisting of rheumatoid arthritis, multiple sclerosis and systemic lupus erythematosis.

46. A method for treating a cancer in a mammal suffering from a cancer comprising the step of treating the mammal with a therapeutically effective amount of the polypeptide according to any one of claims 1-22.

47. The method according to claim 46, wherein said cancer is selected from the group consisting of leukemia, lymphoma, or multiple myeloma.

48. The method according to claim 46, wherein said cancer is a gastrointestinal cancer or a glioblastoma.

49. A method for treating a T-cell mediated disease in a mammal suffering from a T-cell mediated disease comprising the step of treating the mammal with a therapeutically effective amount of the polypeptide according to any one of claims 1-22.

50. The method according to claim 49, wherein the T-cell mediated disease is selected from the group consisting of graft rejection, graft verses host disease (GVHD) and inflammation.